REMARKS

After entry of this Amendment, claims 1, 5, 9, 51 and 59 will be pending in this application.

Claims 1, 5, 9 and 51 have been amended. Claim 59 has been added. Support for the claim amendments and the new claim can be found throughout the specification, particularly at page 12, lines 12-14; page 13, lines 17-22; page 15, lines 2-4; and page 15, line 23 through page 16, line 2. None of the claim amendments adds any new matter to the application.

The undersigned thanks the Examiners Marschel and Smith for taking the time to participate in a telephonic interview on August 3, 2004 to discuss the outstanding rejection under 35 U.S.C. §112.

Rejections under 35 U.S.C. §112, first paragraph

Lack of Scope of Enablement

The Examiner has rejected the pending claims stating that the specification, "while enabling for identifying certain organisms, does not reasonably provide enablement for the identification of any type of pathogen."

Applicants traverse and respectfully submit that the amended claims are enabled throughout their scope. The amended claims recite methods of aiding in the identification or diagnosis of a pathogen based on the expression of pathogen-specific genes. The fact that some experimentation may be necessary to carry out the claimed methods does not preclude enablement, so long as the amount of experimentation required is not undue. Applicants respectfully submit that in this case the amount of experimentation required is not undue since the specification teaches with specificity how the claimed methods can be carried out.

The methods necessary to carry out the invention claimed, namely methods of aiding in the identification or diagnosis of pathogens based on the identification of pathogen-specific genes, are well known in the art. The identification of these genes involves: contacting immature dendritic cells with a pathogen, isolating mRNA from the dendritic cells that have

been contacted by the pathogen, determining the gene expression profiles of said dendritic cells and subsequently analyzing the gene expression profiles from said dendritic cells to identify pathogen-specific genes. All of these methods are all well-known in the art. These methods remain unchanged regardless of the pathogen in question, and the specification specifically exemplifies these methods with respect to three very different pathogens: *E. coli* (a bacteria), *C. albicans* (a fungus) and influenza (a virus). Thus, although some experimentation might be required in order to identify pathogens which are not specifically disclosed in the specification, Applicants submit that the experimentation required would not be undue.

As stated by the Examiner, the *Wands* factors considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, and (7) the predictability or unpredictability of the art. Further, it is well settled that all of the *Wands* factors need not be considered in all instances: what is relevant depends on the facts of each case. *See, e.g., Enzo Biochem., Inc. v. Calgene, Inc.*, 188 F.3d 1363, 1371 (Fed. Cir. 1999).

In this case, the quantity of experimentation necessary is not undue. The specification provides direction in all of the methodology necessary to carry out the invention. *See, e.g.*, page 12, lines 22-25 (stating that methods of isolating mRNA and determining gene expression profiles are well known in the prior art); page 14, line 26 through page 14, line 15 (describing how pathogen-specific genes are identified); page 19, line 21 through page 21, line 18 (providing a detailed explanation of how dendritic cells are contacted with pathogens, their mRNA isolated and their gene expression profiles obtained); and Examples 1-3. Further, the specification provides at least three working examples which confirm that the claimed methods can be carried out with respect to three very different pathogens. Moreover, the level of skill in the art is high, and a person having skill in the art would be familiar with the methods used to carry out the invention. Thus, although the scope of the claims is broad, the disclosure in the specification and the knowledge of the skilled artisan are commensurate with the scope of the claims. The Examiner notes in the Office Action (page 3) that "adequate working examples and direction were presented for the bacterium fungus, and virus." Accordingly, Applications respectfully submit that the evidence as a whole demonstrates that the pending claims are enabled throughout

their scope. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Lack of Enablement

Further, the Examiner states that the pending claims lack enablement because the "very broad assertion [that pathogens can be identified by noting stimulus-specific genes that are specific to a particular pathogen] cannot stand based solely on the three types of pathogens tested." The Examiner also states that "one of skill in the art cannot automatically conclude that [a] modification in [gene] expression [after implementing a stimulus] also indicates infection has occurred without further experimentation to verify this assertion."

Applicants traverse and respectfully submit that the amended claims, directed to methods of *aiding* in the identification or diagnosis of pathogens, are enabled as explained above. The amended claims do not require that the detection of a pathogen-specific gene is 100% indicative of the presence of the pathogen. Rather, the amended claims only require that the detection of a pathogen-specific gene aids in the identification/diagnosis of a pathogen, i.e., as one factor to identify the pathogen. Support for this amendment can be found in the specification which states that the present invention "aids in the identification of known and novel pathogens" (page 12, lines 12-14).

Further, the Examiner states that "none of the method steps in these claims mentions a comparison to a control which is paramount to equating a gene to a particular association during gene expression analysis." Applicants' amendments to claims 1, 5, 9 and 51 obviate this rejection.

Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Rejections under 35 U.S.C. §103

The Examiner has rejected the pending claims over Cummings *et al.*, *Genomics* 6(5):513-525 (2000) ("Cummings") in view of Hashimoto *et al.*, *Blood* 96(6):2206-2214 (2000) ("Hashimoto") and Cirillo (WO02/08418).

Applicants respectfully traverse. Cummings does not disclose or suggest the claimed methods of aiding in the identification or diagnosis of pathogens based on the expression of pathogen-specific genes in dendritic cells.

Cummings states that "host profiling *might* identify gene expression signatures unique pathogen" (abstract; emphasis added), and concludes that "the goal of these experiments (to define unique signatures for each pathogen) has not yet been realized" (page 522, first column, first full paragraph). Thus, Cummings makes clear that at the time it was published no one had identified a gene expression signature that could be used to identify particular pathogens.

Further, nothing in Cummings discloses or suggests looking at the expression of pathogen-specific genes in dendritic cells to aid in the identification or diagnosis of pathogens. Applicants respectfully submit that the use of dendritic cells is an essential element of the claimed invention which is not disclosed by Cummings. Dendritic cells are important to the invention because of their role in antigen presentation. The Examiner states (page 11) that Cummings "describes examining the response of human promyelocytic cells [] which are immature myelocytes that can be nerve cells while dendritic cells include nerve cells which provides evidence of studying similar types of cells" Applicants respectfully submit that the Examiner is confusing dendritic cells (which are immune cells) with dendrites (which are nerve cells). This confusion may have arisen due to the use of the term "dendritic" which can be defined as "branched like a tree" or "pertaining to or possession dendrites." (*See* Exhibit A.) "Dendrites" are extensions of neurons (nerve cells) which carry electric signals between cells (Exhibit B). "Dendritic cells" on the other hand are specific types of cells in the immune cell (Exhibits C and D). One reference (www.wikipedia.com; Exhibit D) defines dendritic cells as follows:

> Dendritic cells are immune cells and form part of the mammal immune system. They are present in those tissues which are in contact with the environment: in the skin [] and the lining of nose, lungs, stomach and intestines. They have long spiky arms, called dentrites, hence the name. (Neurons also have dendrites, but dendritic cells have nothing to do with neurons.)

Further, the specification clearly defines dendritic cells (page 1, line 4 through page 2, line 6) and immature dendritic cells (page 19, lines 23-24). Thus, nothing in Cummings discloses or suggests using dendritic cells to examine host-pathogen interactions.

The Examiner appears to believe that one of ordinary skill in the art would have been motivated to combine the teachings of Cummings and Hashimoto to perform the methods disclosed in Cummings on dendritic cells. Applicants respectfully traverse. Hashimoto discloses the use of serial analysis of gene expression ("SAGE") to identify genes which are involved in the maturation of dendritic cells, since LPS stimulates the maturation of dendritic cells. Hashimoto does not disclose or suggest the use of dendritic cells to identify or diagnose pathogens. Further, there is no motivation to combine the teachings of Hashimoto with the teachings of Cummings.

Cirillo does not cure the deficiencies of Cummings and Hashimoto. Cirillo, at most, teaches the use of two specific genes to identify *Legionella pneumophila* bacteria in a subject by obtaining mRNA from monocytes and probing for the detection of such genes. Nothing in Cirillo teaches or suggests methods of aiding in the identification of a pathogen by detecting pathogen-specific genes in mRNA isolated from dendritic cells. Further, there is no motivation to combine the teachings of Cirillo with the teachings of Cummings.

Finally, assuming *arguendo* that a person of ordinary skill in the art would have been motivated to combine the teachings of Cummings and Hashimoto or Cirillo, there would have been no reasonable expectation of success since Cummings explicitly states that at the time this reference was published no one had been able to identify unique gene signatures for pathogens.

Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendment, Applicants believe the pending application is in condition for allowance, and is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Applicants believe no fee is due with this response other than the fee for filing an RCE. However, if a fee is due, please charge our Deposit Account No. 18-1945, from which the undersigned is authorized to draw, under Order No. WIBL-P01-548.

Dated: August 11, 2004

Respectfully submitted,

By 

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